CHAPTER I

INTRODUCTION

For systemic delivery, the oral route has been the preferred route of administration for many systemically active drugs. However, many therapeutic agents are reportedly subjected to extensive presystemic elimination by gastrointestinal degradation and/or hepatic metabolism. Results of low systemic bioavailability, short duration of therapeutic activity were observed. Delivery of drugs via the absorption mucosa in various easily accessible body cavities like rectal mucosa has the advantages over oral therapy. For example, drugs destroyed or inactivated by the pH or enzymatic activity of the stomach or intestines need not be exposed to these destructive environments, Drugs destroyed by portal circulation may bypass the liver after rectal absorption (drug enters the portal circulation after oral administration and absorption). This route is convenient for administration of drugs to adult or pediatric patients who may be unable or unwilling to swallow medication. It is also an effective route in the treatment of patients with vomiting episodes.

However, rectal suppositories have many limitations particularly in storage condition. Because they can melt at room temperature, it is necessary to keep them in the refrigerator. In Thailand, which is the tropical country, using or carrying and storaging suppositories become inconvenient to patients.

Many researchers have found the ways to overcome these problems and one of them is the use of rectal capsule. Rectal capsule, also known as shell suppository is generally similar to soft gelatin capsule. Although the soft gelatin capsule can be use as rectal capsule (Axel and Christel, 1997), many researchers are interested in using hard gelatin capsule due to advantage of thinner capsule shell and ease of preparation (Cade et al., 1986). Many publishers showed satisfactory results from the investigation of hard gelatin capsule as a rectal dosage form. It was found, for example, that ibuprofen

capsule could provided adequate drug in blood level via rectal route (Eerikaunen et al., 1996 ; Leino et al., 1997).

In the present study, ketoprofen was selected as a model drug for development of a rectal capsule dosage form. Ketoprofen is a nonsteroidal drug that has been clinically proven to be an effective and potent anti-inflammatory agent with analgesic and antipyretic properties. Like other nonsteroidal anti-inflammatory drugs, oral administration of ketoprofen can develop risks of gastrointestinal irritation, bleeding, nausea and vomiting. To minimize these complications, an alternative way of administering such a drug could be possibly the rectal route (Shimpo et al., 1981).

Objectives of this study

1. To formulate 100 mg ketoprofen liquid filled in coated hard gelatin capsule for rectal use.
2. To evaluate *in vitro* release characteristics of ketoprofen from 100 mg ketoprofen liquid filled in coated hard gelatin capsule.
3. To investigate bioavailability of ketoprofen liquid filled in coated hard gelatin capsule for rectal use in rabbits.